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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/574,460	05/18/2000	Michael A. Apicella	17023.004US1	6817

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
07/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/574,460	APICELLA ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30,34,37-39,43,46-48 and 54-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30, 34, 37-39, 43, 46-48 and 54-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 12, 2007, amending claims 30, 39 and 48 and canceling claims 31-33, 40-42, 44-45, 40-50 and 52-53, has been entered.

Claims 30, 34, 37-39, 43, 46-48 and 54-58 are pending and are under consideration.

The use of the trademarks has been noted in this application, for example, "Pharmacia", page 12, line 13. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Applicant's cooperation is requested in reviewing the specification for additional trademarks that may be present in the specification and making the appropriate correction(s).

Response to Arguments

Applicant's amendment and arguments filed on April 12, 2007, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30, 34, 37-39, 43, 46-48 and 54-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 30, 34, 37-39, 43, 46-48 and 54-58 are drawn to a method of producing a lipooligosaccharide (LOS) or complex carbohydrate by culturing a *Salmonella minnesota* comprising a polynucleotide encoding an undecaprenyl-phosphate N-acetyl glucosaminyl phosphate transferase (rfe), wherein said bacteria is transformed with a polynucleotide encoding a lipooligosaccharide-synthesis gene G polypeptide (lsgG)

from *H. influenzae*, wherein a terminal heptose of a lipopolysaccharide (LPS) or LOS core structure of said gram-negative bacterial species is modified by the addition of N-acetyl glucosamine. The claims encompass a method of producing LOS by transforming *S. minnesota* with any or all polynucleotides encoding a LsgG from *H. influenzae*, including any or all variants, mutants and recombinants thereof, wherein said *S. minnesota* endogenously comprises any or all polynucleotides encoding a rfe or are transformed with any or all polynucleotides encoding a rfe from another including any or all variants, mutants and recombinants thereof. Therefore, the claims are drawn to a method of producing LOS using a *S. minnesota*, wherein (A) said bacterium is transformed with a genus comprising any or all polynucleotides encoding a LsgG from *H. influenzae,* having any structure and (B) said bacterium endogenously produces rfe or is transformed with a genus of any or all polynucleotides encoding a rfe from any source having any structure.

The specification only describes a method of producing specific LOS described in Table 2 and 3 by transforming *S. minnesota* with a polynucleotide encoding lsgG isolated from *H. influenzae (*pGEMLOS-4, pGEMLOS-5 or PGEMLOS-7), wherein the polynucleotide encoding rfe is endogenous to the bacteterium. This one example is not enough and does not constitute a representative number of species to describe the whole a method of making LOS in *S. Minnesota* by using a genus comprising any or all polynucleotides encoding rfe or genus comprising any or all polynucleotides encoding lsgG. There is no evidence on the record of the relationship between the structure of the polynucleotide encoding lsgG in pGEMLOS-4 and the structure of any or all

polynucleotides encoding lsgG, including any or all recombinants, mutants and variants thereof. Similarly, there is no evidence on the record of the relationship between the structure of the polynucleotide encoding rfe endogenous to *S. minnesota* and the structure of any or all polynucleotide encoding rfe, including any or all recombinants, mutants and variants thereof. Therefore, the specification fails to describe a representative species of the genus comprising any or all polynucleotides encoding rfe and genus comprising any or all polynucleotides encoding lsgG and used to transform a *S. minnesota* to produce LOS.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 30, 34, 37-39, 43, 46-48 and 54-58.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office Action, applicants have traversed the above rejection. Applicants should note that the rejection has been amended in light of the amendment of the claims.

Applicants argue that when the claims recite a known gene, applicant need not recite the level of detail that would be required if one were claming a previously-unknown gene. Examiner respectfully disagrees. The claims are not limited to only wild

type genes known in the art, but to a method of producing LOS using a *S. minnesota*, wherein (A) said bacterium is transformed with a genus comprising any or all polynucleotides encoding a LsgG from *H. influenzae,* having any structure and (B) said bacterium endogenously produces rfe or is transformed with a genus of any or all polynucleotides encoding a rfe from any source having any structure. The recitation of "LsgG" and "rfe" fails to provide a sufficient description of the claimed genus of polynucleotides encoding polypeptides as it merely describes the functional features of the encoded polypeptides of the genus without providing any definition of the structural features of the species within the genus. The CAFC in UC California v. Eli Lilly, (43 USPQ2d 1398) stated that: "in claims to genetic material, however a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus." Similarly with the claimed genus of "LsgG" and "rfe" polynucleotides, the functional definition of the genus does not provide any structural information commonly possessed by members of the genus which distinguish the protein species within the genus from other proteins such that one can visualize or recognize the identity of the members of the genus. Further, as discussed in the written description guidelines, the written description requirement for a claimed

genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genus includes species which are widely variant in structure. As such, the disclosure of solely functional features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus.

Hence the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 30, 34, 37-39, 43, 46-48 and 54-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over McLaughlin et al. in view of Preston et al. and Swierzko et al.

Claims 30, 34, 37-39, 43, 46-48 and 54-58 are drawn to a method of producing LOS or complex carbohydrate and a method of adding a N-acetyl glucosamine to a terminal heptose of a LOS or LPS core structure using a *S. minnesota* transformed with a polynucleotide encoding a rfe from *H. influenzae* and a polynucleotide encoding a LsgG from *H. influenzae*.

McLaughlin et al. (form PTO-1449) discloses to a method of producing LOS, a complex carbohydrate, using an *E. coli* transformed with a polynucleotide encoding a lsgG from *H. influenzae,* wherein said *E. coli* endogenously comprises a polynucleotide encoding a rfe polynucleotide (pages 165-166). In the method of McLaughlin et al., N-acetyl glucosamine is added to a terminal heptose of a LOS or LPS core structure. With this teaching at hand, one having ordinary skill in the art would have looked to

apply the method of McLaughlin et al. in other bacterium comprising a terminal heptose molecule.

The difference between the reference of McLaughlin et al. and the instant invention is that the reference of McLaughlin et al. does not teach a method of producing LOS in *Salmonella minnesota*.

Swierzko et al. (cited previously on form PTO-892) discloses that *S. minnesota* bears a terminal heptose molecule, similar to *E. coli*, and discloses using this bacterium in synthesizing LPS (pages 3216-3217). Brade et al. (form PTO-1449) discloses a method of transforming *S. minnesota* with recombinant polynucleotides (page 483).

Preston et al. (form PTO-1449) discloses several genes involved in LOS biosynthesis, including the lsg gene and rfe gene isolated from *H. influenzae* (Table page 154). Preston et al. teaches that *H. influenzae* produce LOS lacking O-antigens, which are present in LPS produced by most Gram-negative bacteria. Alexander et al. (from PTO-1449) confirms said teaching by disclosing that the rfe gene isolated from *E. coli* is involved in O-antigen synthesis of LPS (page 7079, abstract).

Regarding regulation of *rfe* by lsgG, regulation of rfe by LsgG is an inherent property of LsgG, which would flow naturally when both polynucleotides are present.

Therefore, in combining the teachings of McLaughlin et al. Preston et al., Brade et al. and Swierzko et al, it would have been obvious to one having ordinary skill in the art modify the method of McLaughlin et al. by transforming *S. minnesota* et al. with the rfe gene of Preston et al. in addition to the lsg gene. One of ordinary skill in the art would have been motivated to use the rfe gene of Preston et al. in *S. minnesota*

bacterium producing LPS with O-antigens, in order to produce LOS, which lack O-antigens in their structure. One of ordinary skill in the art would have had a reasonable expectation of success since Preston et al. teaches a rfe gene and Swierzko et al. teaches using *S. minnesota* to produce LOS and Brade et al. teaches transformation of *S. minnesota*.

Therefore, the above references render claims 30, 34, 37-39, 43, 46-48 and 54-58 *prima facie* obvious to one of ordinary skill in the art.

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Yong D. Pak
Patent Examiner 1652